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On the scope of diastereoselective aziridination of various chiral auxiliaries derived *N*- and *O*-enones with *N*-aminophthalimide in the presence of lead tetraacetate

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Abstract—The treatment of a range of *N*- and *O*-enones derived from various camphor-based chiral auxiliaries **A**–**D** with *N*-aminophthalimide in the presence of lead tetraacetate is described. In general, *N*-phthalimidoaziridines were obtained with high diastereoselectivities (up to 98% de) and chemical yields (up to 95%) when 10,10-diphenyl-2,10-camphanediol **A** derived *O*-enones with a range of substituents were used under the same reaction conditions. Excellent stereoselectivity was obtained when the *N*-tosyl camphorpyrazolidinone **E** derived acrylate was used. The absolute configuration of the new stereogenic center(s) of the major diastereomer was established by X-ray crystallographic analysis. Chiral auxiliary cleavage was achieved under mild reaction conditions. A model to explain the stereochemical induction is also proposed.

1. Introduction

The synthesis of aziridine derivatives has received much attention as they are important molecules as key components of many biologically active natural products such as mitomycins, which display potent antitumor and antibiotic activity, and are also useful synthetic intermediates for nitrogen-containing compounds.[1] In addition, aziridines are highly versatile synthetic precursors and have been used as synthons for chiral amines, amino acids, β-aminosulfonic acids, amino alcohols, alkaloids, and β-lactam antibiotics.[2] Aziridines are the nitrogen analogues of epoxides and exhibit similar reactivity patterns as electrophilic reagents.[3] It is not surprising that much effort has been devoted to developing efficient methods for the construction of the constrained three-membered ring system.[4] Among the many routes that have been developed, the reaction of nitrenes to olefins or carbenes to imines has potential.[5] The enantioselective and diastereoselective syntheses of non-racemic aziridines have constantly reported in the literature.[6] The Oppolzer camphorsultam is among the most widely used chiral auxiliary in diastereoselective synthesis.[7] In continuation of our research interest in asymmetric synthesis, four novel camphor-derived auxiliaries: 10,10-diphenyl-2,10-camphanediol **A**, 10,10-diphenyl-10-methoxy-2-camphanol **B**, *N*-phenyl camphorpyrazolidinone **C**, and *N*-tosyl camphorpyrazolidinone **D** have been developed and utilized in various asymmetric reactions.[8] Recently, we have reported the diastereoselective aziridination of *N*-enones derived from *N*-phenyl camphorpyrazolidinone with *N*-aminophthalimide in the presence of lead tetraacetate.[9] High to excellent stereoselectivities of the desired aziridines were obtained. In addition, the N-inversion phenomena was observed for *N*-phenyl camphorpyrazolidinone derived *N*-phthalimidoaziridines.[9] Based on these studies, we herein report on the scope of the diastereoselective aziridination of *N*- and *O*-enones **1a**–**o** derived from various camphor-based chiral auxiliaries **A**–**D**. Generally, the desired aziridines were obtained with high stereoselectivities and chemical yields under mild reaction conditions. The stereochemical inductions of the reaction were proposed based on the conformational preference of the chiral *N*- and *O*-enones in their solid state structures.

2. Results and discussion

The starting chiral *O*- **1a**–**k** and *N*-enones **1l**–**1o** can be easily prepared from the corresponding chiral auxiliaries

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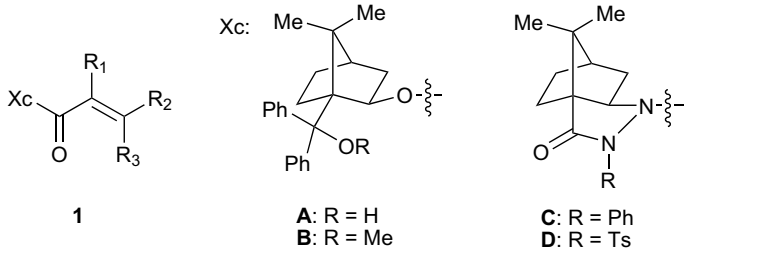
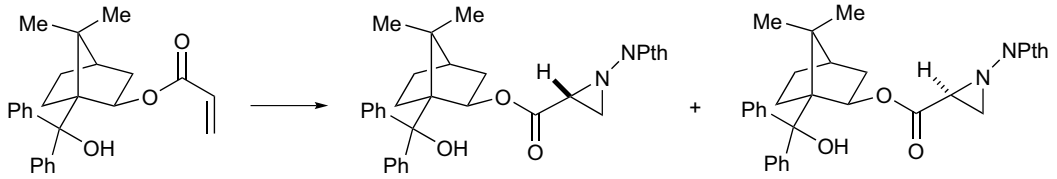
A–**D** by using standard coupling reaction conditions (Fig. 1). With the various *N*- and *O*-enones **1a**–**o** in hand, we then investigated the diastereoselective aziridination reaction using *N*-aminophthalimide in the presence of lead tetraacetate. Vederas et al. have explored the aziridination by using *N*-enoylbornane[10,2]sultams in the presence of *N*-aminophthalimide and lead tetraacetate. The corresponding *N*-phthalimidoaziridines were obtained with 33–95% de.[10] In an initial experiment, 10,10-diphenyl-2,10-camphanediol derived acrylate **1a** was chosen as a probe substrate under the optimal oxidation reaction conditions that were developed previously.[9] Unsatisfactory results (47% yield and 56% de) were obtained when **1a** was treated with *N*-aminophthalimide and lead tetraacetate in CH_2Cl_2 at ambient temperature (Table 1, entry 1). A slight improvement in both chemical yield and stereoselectivity was observed when the reaction was carried out at 0 °C (Table 1, entry 2). The solvent effects were then studied. High stereoselectivity was obtained when the reaction was carried out in $CHCl_3$ (Table 1, entry 3). Comparable results were achieved when CH_3CN was used (Table 1, entry 4). Satisfactory results were obtained when non-polar solvents (benzene and toluene) were used (Table 1, entries 5 and 6). Further improvements in material yield were observed when the reaction was carried out in THF at 0 °C (entry 7). It was obvious that THF is a solvent of choice for this reaction. The structure of the major *N*-phthalimidoaziridine **2a** was initially assigned by ^1H, ^{13}C NMR, and HRMS analyses, and the absolute stereochemistry was assigned as (1*R*) by analogy. The diastereomeric excess was deduced from the relevant peak in the ^1H NMR spectrum of the crude mixture. The characteristic feature of the C2 methine proton (camphor numbering) of the corresponding *N*-phthalimidoaziridines **2** provides a convenient way to assign the stereoselectivity. For example, the C2 methine in **2a** appeared at 5.28 ppm (dd, $J = 8.4$, 3.8 Hz), while it showed up at 5.12 ppm in the minor product **3a**. On the other hand, the aziridine ring protons in **2a** showed up at 2.91 (dd, 1H, $J = 7.8$, 5.4 Hz), 2.62 (dd, 1H, $J = 7.8$, 1.8 Hz), and 2.48 (dd, 1H, $J = 5.4$, 1.8 Hz) ppm, respectively.



1a : X_c = **A**, R_1 = R_2 = R_3 = H
1b : X_c = **A**, R_1 = H, R_2 = Me, R_3 = H
1c : X_c = **A**, R_1 = H, R_2 = Et, R_3 = H
1d : X_c = **A**, R_1 = H, R_2 = *n*-pr, R_3 = H
1e : X_c = **A**, R_1 = H, R_2 = *i*-pr, R_3 = H
1f : X_c = **A**, R_1 = H, R_2 = Ph, R_3 = H
1g : X_c = **A**, R_1 = Me, R_2 = R_3 = H
1h : X_c = **A**, R_1 = R_2 = Me, R_3 = H
1i : X_c = **A**, R_1 = Me, R_2 = Et, R_3 = H
1j : X_c = **A**, R_1 = H, R_2 = R_3 = Me
1k : X_c = **B**, R_1 = H, R_2 = Me, R_3 = H
1l : X_c = **C**, R_1 = R_2 = R_3 = H
1m : X_c = **C**, R_1 = H, R_2 = Me, R_3 = H
1n : X_c = **D**, R_1 = R_2 = R_3 = H
1o : X_c = **D**, R_1 = H, R_2 = Me, R_3 = H

Figure 1.

Table 1. Asymmetric aziridination of 10,10-diphenyl-2,10-camphandiol derived acrylate **1a** with *N*-aminopthalimide in the presence of lead tetraacetate[a]



1a (Xc = A) **2a** (Xc = A) **3a** (Xc = A)

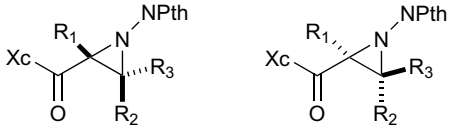
Entry	Solvent	*T*	Yield (%)	Ratio (**2a**:**3a**)
1	CH_2Cl_2	rt	47	78:22
2	CH_2Cl_2	0 °C	53	86:14
3	$CHCl_3$	0 °C	68	94:06
4	CH_3CN	0 °C	75	94:06
5	Benzene	>5 °C	71	94:06
6	Toluene	0 °C	73	88:12
7	THF	0 °C	90	94:06

[a] All reactions were performed using chiral enone **1a** (0.2 g, 0.53 mmol), *N*-aminophthalimide (1.5 equiv), $Pb(OAc)_4$ (1.6 equiv) in THF (5.0 mL) at 0 °C.

Various 10,10-diphenyl-2,10-camphanediol derived *O*-enones with α-, β-, α,β-di, and β,β-disubstituent(s) were then subjected to the optimal reaction conditions. Moderate stereoselectivities were obtained when acryoyl *O*-enones **1b** was used (Table 2, entry 1). High stereoselectivities and material yields were obtained when other β-substituents (ethyl-, *n*-propyl-, and isopropyl-) were used (Table 2, entries 2–4). The electron-rich *O*-cinnamoyl enone **1f** was investigated and the desired products were isolated with 75% yield and 80% de (Table 2, entry 5). The stereoselectivity dropped significantly when an α-substituent is present. The α-substituent effect on the yield has been observed before.[10] The α-substituent effect may come from the deviation of dihedral angle from the planar geometry of the enone. The α-substituent effect does not influence the reactivity in the case of 10,10-diphenyl-2,10-camphanediol derived *O*-enones. However, it does affect the stereoselectivity. Thus, the use of *O*-methacryloyl enone **1g** gave only moderate stereoselectivity (**2g**:**3g** = 61:39) (entry 6). Interestingly, the selectivity rebounds with the presence of an additional β-substituent. Toward this end, high stereoselectivities were obtained when α,β-dimethyl **1h** and α-methyl β-ethyl **1i** substrates were used under the same reaction conditions (Table 2, entries 7 and 8). Similar result was observed when β, β-dimethyl substituent **1j** was used (Table 2, entry 9). A similar observation was noted when *N*-phenyl camphorpyrazolidinone derived *N*-enone was used.[9] The absolute stereochemistries of the major isomeric products of **2b**–**f** were confirmed by single crystal X-ray analyses. Next, the use of 10,10-diphenyl-10-methoxy-2-camphanol **B** derived *O*-enone was also studied. The desired product **2k** was obtained with 74% de in favoring the (1*R*,2*S*)-configuration of the newly generated aziridine ring (Table 2, entry 10). The use of *N*-phenyl camphorpyrazolidinone **C** derived *N*-enones **1l** and **1m** gives the desired aziridine with high selectivities (Table 2, entries 11 and 12).[9] Further, the treatment of *N*-tosyl camphorpyrazolidinone **E** derived acrylate **1n** with *N*-aminophthalimide in the presence of lead tetraacetate afforded **2n** with >95% de (Table 2, entry 13).

As mentioned, Vederas et al. have reported the aziridination of *N*-enoylbornane[10,2]sultams with *N*-aminophthalimide in the presence of lead tetraacetate. The corresponding *N*-phthalimidoaziridines were obtained with 33–95% de in good to high material yields.[10] Comparison of the aziridination of the camphorsultam derived *N*-enones and the current results indicate auxiliaries **A**–**D** providing better stereofacial discrimination. For example, the aziridination of camphorsultam derived acrylate ($R_1 = R_2 = R_3 = H$) gave the corresponding *N*-phthalimidoaziridines with 78% de, while with 88%, >90%, and >90% de, respectively when auxiliaries **A**, **C**, and **D** derived acrylates were used (Table 1, entry 7 and Table 2, entries 11 and 13). Moreover, for auxiliaries **A**–**D** derived from *N*-crotonyl substrates ($R_1 = H$, $R_2 = Me$, $R_3 = H$), the diastereoselectivities (64–90% de; Table 2, entries 1, 10, 12, and 14) are also better than those of *N*-crotonyl camphorsultam (33% de).

Table 2. Asymmetric aziridination of various enones **1b**–**o** with *N*-aminopthalimide in the presence of lead tetraacetate[a]



2b-o **3b-o**

Entry	Substrate	Time (min)	Yield[b] (%)	Ratio (**2**:**3**)[c]	Configuration[d]
1	**1b** Xc = A, $R_1 = H$, $R_2 = Me$, $R_3 = H$	40	90	82:18	(1*R*,2*S*)
2	**1c** Xc = A, $R_1 = H$, $R_2 = Et$, $R_3 = H$	5	95	93:07	(1*R*,2*S*)[e]
3	**1d** Xc = A, $R_1 = H$, $R_2 = n$-Pr, $R_3 = H$	5	90	93:07	(1*R*,2*S*)
4	**1e** Xc = A, $R_1 = H$, $R_2 = i$-Pr, $R_3 = H$	5	95	95:05	(1*R*,2*S*)
5	**1f** Xc = A, $R_1 = H$, $R_2 = Ph$, $R_3 = H$	15	75	90:10	(1*R*,2*S*)
6	**1g** Xc = A, $R_1 = Me$, $R_2 = R_3 = H$	10	95	61:39	(1*R*)[e]
7	**1h** Xc = A, $R_1 = R_2 = Me$, $R_3 = H$	5	95	95:05	(1*R*,2*S*)
8	**1i** Xc = A, $R_1 = Me$, $R_2 = Et$, $R_3 = H$	5	95	95:05	(1*R*,2*S*)[e]
9	**1j** Xc = A, $R_1 = H$, $R_2 = R_3 = Me$	10	70	05:95	(1*S*)[e]
10	**1k** Xc = B, $R_1 = H$, $R_2 = Me$, $R_3 = H$	5	90	87:13	(1*R*,2*S*)[e]
11[f]	**1l** Xc = C, $R_1 = R_2 = R_3 = H$	5	94	>95:05	(1*R*)
12[f]	**1m** Xc = C, $R_1 = H$ $R_2 = Me$, $R_3 = H$	5	90	>95:05	(1*R*,2*S*)
13	**1n** Xc = D, $R_1 = R_2 = R_3 = H$	10	50	>95:05	(1*R*)
14	**1o** Xc = D, $R_1 = H$, $R_2 = Me$, $R_3 = H$	10	53	>95:05	(1*R*,2*S*)[e]

[a] Unless otherwise noted, all reactions were performed using chiral enones (0.2 g), *N*-aminophthalimide (1.5 equiv), $Pb(OAc)_4$ (1.6 equiv) in THF (5.0 mL) at 0 °C.

[b] Total isolated yield (**2** and **3**).

[c] Diastereoselectivity was determined by ^1H NMR analysis of relevant peaks of crude products.

[d] Absolute stereochemistry of the newly generated stereogenic centers deduced by single X-ray crystal analyses.

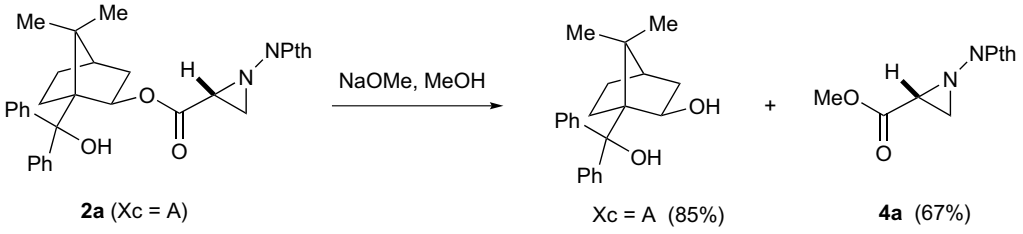
[e] Absolute stereochemistry was assigned by analogy.

[f] See Ref. 9.

An interesting N-interconversion phenomena of *N*-phthalimidoaziridine was observed by both us and Atkinson et al.[9,11] The kinetically formed *trans*-aziridine **2l** inverts at the aziridine nitrogen atom to the thermodynamically preferred *cis*-aziridine. Similar phenomena were observed for *N*-methacryloyl 10,10-diphenyl-2,10-camphanediol derived aziridine **2g**. Thus, the isolated pure diastereomer of **2g** (flash column chromatography, E. Merck Silica Gel 60, $R_f = 0.4$, hexanes/ethyl acetate = 4:1) slowly converts into its less polar N-invertomer ($R_f = 0.6$, hexanes/ethyl acetate = 4:1) and reached an equilibrium to give a 3:2 ratio at ambient temperature over 30 min. The ^{1}H NMR spectra of both diastereomers are identical in $CDCl_3$. It is pertinent to note that *N*-tosyl camphorpyrazolidinone derived acrylate **1n** produced exclusively one diastereomer with moderate yield (Table 2, entry 13). The absolute configuration of the newly generated stereogenic center was established as (1*R*) by single X-ray crystal analysis. The rapid equilibrium of N-interconversion was also observed for **1n** ($R_f = 0.1$ and 0.3, hexanes/ethyl acetate = 4:1). To complete one cycle of the chiral auxiliary, the initial adduct was subjected to deacylation conditions. Exposure of **2a** with NaOMe in methanol at ambient temperature provided the desired 2-carboxyl aziridine derivative **4a** (67%) {$[\alpha]_D = +109.5$ (*c* 1, $CHCl_3$)} and 10,10-diphenyl-2,10-camphanediol **A** was recovered in 85% yield (Scheme 1).

The aziridination reaction using *N*-aminophthalimide in the presence of lead tetraacetate proceeded with a non-chelation fashion. The stereochemical induction can be rationalized based on the conformational structures of the auxiliaries derived *N*- and *O*-enones (Fig. 2). The relationship of reaction rate/stereoselectivity and geometry arrangement of camphorsultam conjugated *N*-enones have been examined by both Oppolzer[12] and Curran.[13] For amide derived *N*-enone functionality, the *s-cis* conformation dominates with no substituent and β-substituents while favoring the *s-trans* disposition if an α-substituent is present. For example, α,β-substituted *N*-enones **1l** energetically favor *s-trans* geometry, while for β-substituted *N*-enone **1m**, planar *s-cis* conformation dominate.[9,13,14] In contrast to the amide *N*-enone **C** and **D** system, the ester linkage *O*-enones exhibit different conformational behaviors. The *s-trans* conformation is energetically favored for the unsubstituted, β-substituent, and an α,β-disubstituted of *exo*-10,10-diphenyl-2, 10-camphane diol **A** derived *O*-enones.[15] This can be confirmed by the single X-ray crystal analyses of compounds **1b–c** and **1g–h**. Interestingly, for β,β-disubstituted *O*-enone **1j**, the *s-cis* conformation is energetically favored as indicated by the single X-ray crystal analysis. Similar to the *N*-phenyl camphorpyrazolidinone **C** derived *N*-enones, the bulky *N*-acetoxyaminophthalimide comes from the less hindered bottom face. For **1a–i**, the attack is from the Cα *re*-face, while from the opposite *si*-face for **1j** to give the observed stereoisomers.

It is important to note that the amide carbonyl group orients away from the sulfonyl group in *N*-tosyl camphorpyrazolidinone **D** derived acrylate **1n**. This is to minimize the dipole–dipole repulsions between the sulfonyl and carbonyl groups. The planar *s-cis* conformation is favored in the solid state (the dihedral angle of C=O–C=C is −4.37). The attack of an *N*-acetoxyaminophthalimide intermediate from the Cα *re*-face gives the desired major diastereomer. The low levels of asymmetric induction were obtained (Table 2, entry 6) when **1g** was used, may be due to the dihedral angle deviating from planarity (the dihedral angle of C=O–C=C is 152.5).



Scheme 1.

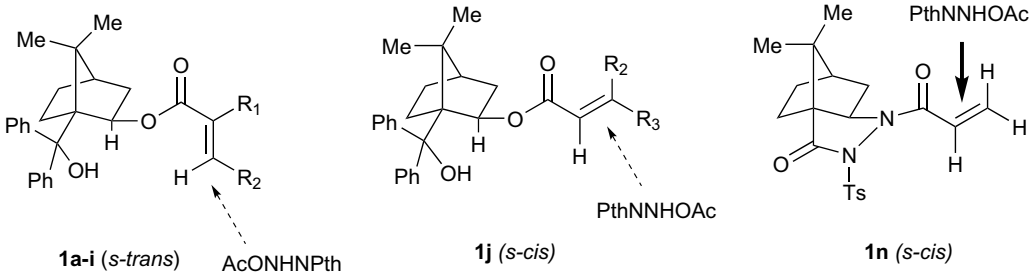


Figure 2. Proposed mechanism for the diastereoselective aziridination of various chiral *O*- and *N*-enones derived from camphor-based auxiliaries.

3. Conclusion

In conclusion, the diastereoselective aziridinations of various *N*- and *O*-enones derived from various chiral auxiliaries have been demonstrated. The treatment of the *O*- and *N*-enones with *N*-aminophthalimide in the presence of lead tetraacetate afforded the corresponding *N*-phthalimidoaziridines with high diastereoselectivities (up to 98% de) and chemical yields (up to 95%). The diastereomeric excess can be determined by the relevant peak in the ^{1}H NMR spectrum (C2 methine proton of the camphor scaffold) of the crude mixtures. The stereochemical bias can be explained by the conformational preference of the starting enones in the solid states. For *exo*-10,10-diphenyl-2,10-camphanediol **A** derived *O*-enones **1a-i**, the addition of the *N*-acetoxyaminophthalimide intermediate attacks from the Cα *re*-face, while from the opposite *si*-face for **1j** to give the observed stereoisomers. On the other hand, for *N*-tosyl camphorpyrazolidinone **D** derived *N*-enones, the oxidation reagent attack from the Cα *re*-face afforded the desired major aziridine.

4. Experimental

4.1. General methods

All reagents were used as purchased from commercial suppliers without further purification. NMR spectra were recorded on a Varian Gemini-2000 200 NMR and Bruker Avance 400 NMR spectrometer (200 and 400 MHz for ^{1}H, and 50 and 100 MHz for ^{13}C). Chemical shifts are reported in δ ppm referenced to an internal TMS standard for ^{1}H NMR and chloroform-*d* (δ 77.0) for ^{13}C NMR. Optical rotations were measured on a JASCO P-1010 polarimeter. EI mass spectra were recorded on Finnigan TSQ-700 at an ionizing energy of 70 eV and HRMS spectra were recorded on MAT-95XL HRMS. Routine monitoring of reactions was performed using silica gel, glass-backed TLC plates (Merck Kieselgel 60 F254) and visualized by UV light (254 nm). Solutions were evaporated to dryness under reduced pressure with a rotary evaporator and the residue was purified by flash column chromatography on silica gel (230–400 mesh) with the indicated eluents. Air and/or moisture sensitive reactions were performed under the usual inert atmosphere conditions.

Crystallographic data for the structures in this paper have been deposited at the Cambridge Crystallographic Data Center and allocated the deposit numbers CCDC 655358–655366.[16]

4.2. General procedure for the synthesis of compounds 1a–k and 1n–o

Under an N_2 atmosphere *exo*-10,10-diphenyl-2,10-camphanediol (1.0 g, 3.1 mmol) and NaH (110 mg, 4.6 mmol) in dry THF (30 mL) were stirred at 0 °C for 20 min. This was added to acryloyl chloride (0.39 mL, 4.6 mmol) dropwise and continued stir for 30 min at 0 °C. The reaction mixture was then quenched with water (75 mL) and extracted with dichloromethane (3 × 50 mL). The combined organic extracts were dried over brine, dried over $MgSO_4$, and concentrated in vacuo. The obtained crude products were subjected to flash column chromatography eluted with hexanes/ethyl acetate 4:1 to afford product **1a** as a white solid (1.03 g, 88%).

4.2.1. Acrylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1a. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.61 (m, 4H), 7.34–7.07 (m, 6H), 6.19–5.70 (m, 3H), 5.24 (dd, 1H, $J = 8.1$, 3.5 Hz), 3.80 (s, 1H), 2.41–2.26 (m, 1H), 2.07–1.50 (m, 8H), 1.24–1.11 (m, 1H), 0.64 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.7, 148.9, 143.4, 130.5, 128.5, 128.0, 127.9, 126.9, 126.5, 126.2, 126.0, 81.8, 81.3, 59.2, 51.3, 47.7, 38.4, 31.0, 26.9, 24.4, 22.5; HRMS (EI): calcd for $C_{25}H_{28}O_3$, 376.2038; found, 376.2049.

4.2.2. But-2-enoic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1b. Yield 78%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.78–7.61 (m, 4H), 7.30–7.05 (m, 6H), 6.68 (dq, 1H, $J = 11.2$, 1.8 Hz), 5.56 (dq, 1H, $J = 15.4$, 1.8 Hz), 5.20 (dd, 1H, $J = 8.1$, 3.7 Hz), 3.93 (1H, s), 2.40–2.25 (m, 1H), 2.05–1.45 (m, 10H), 1.26–1.07 (m, 2H), 0.61 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.9, 148.9, 144.6, 143.4, 128.4, 127.9, 127.8, 126.8, 126.4, 126.1, 126.0, 125.9, 122.1, 81.3, 81.3, 59.0, 51.2, 47.6, 38.5, 30.8, 26.9, 24.4, 22.5, 17.7; HRMS (EI): calcd for $C_{26}H_{30}O_3$, 390.2195; found, 390.2202.

4.2.3. Pent-2-enoic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1c. Yield 73%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.63 (m, 4H), 7.26–7.07 (m, 6H), 6.81–6.67 (dt, 1H, $J = 14.7$, 6.5 Hz), 5.56 (d, 1H, $J = 14.7$ Hz), 5.19 (dd, 1H, $J = 8.0$, 4.0 Hz), 3.94 (s, 1H), 2.38–2.25 (m, 1H), 2.23–1.47 (m, 10H), 1.23–1.10 (m, 1H), 1.03 (t, 3H, $J = 7.3$ Hz), 0.62 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.9, 148.9, 143.6, 137.0, 128.5, 128.3, 127.9, 126.9, 126.5, 126.2, 126.1, 81.6, 81.4, 59.1, 51.3, 47.8, 38.6, 31.0, 27.0, 24.5, 22.6, 14.2, 12.1; HRMS (EI): calcd for $C_{27}H_{32}O_3$, 404.2351; found, 404.2357; Crystal data for **1c** at 25 °C: $C_{27}H_{32}O_3$, $M = 404.54$, orthorhombic, $P2_12_12_1$, $a = 6.931(4)$ Å, $b = 13.806(5)$ Å, $c = 23.533(5)$ Å, $V = 2252.0(15)$ Å^3, $Z = 4$, $D_c = 1.193$ Mg/m^3, $\mu = 0.08$ mm^{-1}, 2293 reflections, 272 parameters, $R = 0.050$, $Rw = 0.146$.

4.2.4. Hex-2-enoic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1d. Yield 88%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.63 (m, 4H), 7.26–7.05 (m, 6H), 6.67 (dt, 1H, $J = 15.6$, 7.0 Hz), 5.54 (dt, 1H, $J = 15.6$, 1.6 Hz), 5.20 (dd, 1H, $J = 7.8$, 3.8 Hz), 3.92 (s, 1H), 2.40–2.25 (m, 1H), 2.14–1.27 (m, 9H), 1.53 (s, 3H), 1.24–1.08 (m, 1H), 0.89 (t, 3H, $J = 7.4$ Hz), 0.62 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 171.0, 164.0, 149.3, 148.8, 143.4, 128.4, 127.8, 126.7, 126.4, 126.1, 126.0, 120.8, 81.2, 60.2, 59.0, 51.2, 47.6, 38.4, 33.9, 30.9, 26.9, 24.4, 22.5, 21.0, 20.8, 14.0, 13.3; HRMS (EI): calcd for $C_{28}H_{34}O_3$, 418.2508; found, 418.2505.

4.2.5. 4-Methyl-pent-2-enoic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1e. Yield 76%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.63 (m, 4H),

7.26–7.06 (m, 6H), 6.65 (dd, 1H, $J = 15.7$, 6.8 Hz), 5.47 (dd, 1H, $J = 15.7$, 1.3 Hz), 5.19 (dd, 1H, $J = 7.9$, 3.9 Hz), 3.92 (s, 1H), 2.06–1.46 (m, 6H), 1.54 (s, 3H), 1.31–0.85 (m, 2H), 1.01 (d, 6H, $J = 6.8$ Hz,), 0.63 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.6, 155.8, 149.0, 143.5, 128.5, 127.9, 126.9, 126.5, 126.3, 126.1, 118.0, 81.5, 81.4, 59.2, 51.3, 47.8, 38.5, 31.0, 30.9, 27.0, 24.5, 22.6, 21.1, 21.0; HRMS (EI): calcd for $C_{28}H_{34}O_3$, 418.2508; found, 418.2517.

4.2.6. 3-Phenyl-acrylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1f. Yield 80%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.80–7.64 (m, 4H), 7.50–7.36 (m, 6H), 7.29–7.05 (m, 6H), 5.28 (dd, 1H, $J = 7.7$, 4.1 Hz), 3.96 (s, 1H), 2.43–2.29 (m, 1H), 2.10–1.50 (m, 5H), 1.58 (s, 3H), 1.26–0.85 (m, 2H), 0.65 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 163.9, 149.2, 148.9, 144.6, 143.5, 143.3, 128.4, 127.9, 127.8, 126.8, 126.4, 126.1, 126.0, 125.9, 122.1, 81.6, 81.3, 59.0, 51.2, 47.6, 38.5, 38.3, 31.0, 30.9, 26.9, 24.4, 22.5, 22.4, 20.7, 17.7; HRMS (EI): calcd for $C_{31}H_{32}O_3$, 452.2351; found, 452.2362.

4.2.7. 2-Methyl-acrylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1g. Yield 83%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.60 (m, 4H), 7.27–7.01 (m, 6H), 5.83 (d, 1H, $J = 1.1$ Hz), 5.46 (d, 1H, $J = 1.1$Hz), 5.27 (dd, 1H, $J = 8.0$, 3.8 Hz), 3.83 (s, 1H), 2.41–2.27 (m, 1H), 2.08–1.49 (m, 5H), 1.77 (s, 3H), 1.54 (s, 3H), 1.26–1.11 (m, 1H), 0.64 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0, 148.9, 143.4, 136.1, 128.5, 127.9, 126.9, 126.5, 126.2, 126.1, 125.1, 81.8, 81.4, 59.2, 51.3, 47.7, 38.5, 31.0, 27.0, 24.4, 22.6, 18.3; HRMS (EI): calcd for $C_{26}H_{30}O_3$, 390.2195; found, 390.2197.

4.2.8. 2-Methyl-but-2-enoic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1h. Yield 57%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75–7.60 (m, 4H), 7.27–7.06 (m, 6H), 6.55 (m, 1H), 5.25 (dd, 1H, $J = 8.0$, 3.6 Hz), 3.96 (s, 1H), 2.40–2.26 (m, 1H), 2.07–1.42 (m, 11H),1.55 (s, 3H) 1.29–1.10 (m, 1H), 0.62 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.8, 148.9, 143.5, 136.9, 128.5, 128.3, 127.8, 126.8, 126.4, 126.2, 126.1, 81.5, 81.4, 59.1, 51.2, 47.7, 38.6, 31.0, 27.0, 24.5, 22.6, 14.2, 12.1; HRMS (EI): calcd for $C_{27}H_{32}O_3$, 404.2351; found, 404.2375.

4.2.9. 2-Methyl-pent-2-enoic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1i. Yield 95%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.75–7.61 (m, 4H), 7.25–7.06 (m, 6H), 6.43 (m, 1H), 5.24 (dd, 1H, $J = 7.9$, 3.7 Hz), 3.92 (s, 1H), 2.40–2.25 (m, 1H), 2.18–1.78 (m, 5H), 1.75–1.20 (m, 8H), 1.17–1.09 (m, 1H), 1.00 (t, 3H, $J = 7.5$ Hz,), 0.63 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.0, 148.9, 143.8, 143.5, 128.4, 127.8, 126.8, 126.6, 126.4, 126.2, 126.0, 81.5, 81.3, 59.1, 51.2, 47.7, 38.5, 31.0, 26.9, 24.5, 22.5, 21.7, 12.8, 12.2; HRMS (EI): calcd for $C_{28}H_{34}O_3$ 418.2508; found, 418.2489.

4.2.10. 3-Methyl-but-2-enoic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1j. Yield 82%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.77–7.63 (m, 4H), 7.27–7.06 (m, 6H), 5.38 (m, 1H), 5.14 (1H, dd, $J = 7.9$, 3.9 Hz), 4.04 (s, 1H), 2.40–2.26 (m, 1H), 1.92(3H, d, $J = 1.2$ Hz), 1.82(d, 3H, $J = 1.4$ Hz), 2.06–1.46 (m, 4H), 1.52 (s, 3H), 1.27–0.85 (m, 2H), 0.60 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.0, 157.5, 149.0, 143.6, 128.5, 127.8, 126.9, 126.3, 126.2, 115.2, 81.3, 80.5, 59.1, 51.2, 47.8, 38.6, 30.9, 27.1, 27.0, 24.5, 22.6, 20.0; HRMS (EI): calcd for $C_{27}H_{32}O_3$, 404.2351; found, 404.2356; Crystal data for **1j** at 25 °C: $C_{27}H_{32}O_3$, $M = 404.54$, orthorhombic, $P2_12_12_1$, $a = 12.621(3)$ Å, $b = 17.873(6)$ Å, $c = 20.580(4)$ Å, $V = 4642.3(20)$ Å^3, $Z = 8$, $D_c = 1.158$ Mg/m^3, $\mu = 0.07$ mm^{-1}, 4521 reflections, 542 parameters, $R = 0.042$, $Rw = 0.093$.

4.2.11. But-2-enoic acid 1-(methoxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 1k. Yield 58%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.82–7.78 (m, 2H), 7.52–7.48 (m, 2H), 7.34–7.19 (m, 6H), 6.21–6.20 (m, 1H), 5.50 (d, $J = 1.6$ Hz, 1H), 4.75 (dd, 1H, $J = 7.7$, 3.1 Hz), 2.80–2.67 (m, 4H), 1.85–1.39 (m, 6H), 1.27–1.23 (m, 4H), 0.95–0.77 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.0, 145.0, 140.0, 139.4, 131.6, 129.5, 127.3, 126.8, 126.7, 126.6, 122.8, 88.0, 80.1, 60.9, 60.2, 52.4, 50.4, 48.7, 39.2, 31.4, 25.2, 23.6, 23.0, 22.5, 17.7, 14.0, 13.9.

4.2.12. 4-Acryloyl-10,10-dimethyl-3-(toluene-4-sulfonyl)-3,4-diaza-tricyclo[5.2.1.0^{1,5}]decan-2-one 1n. Yield 90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (br s, 2H), 7.37 (d, 2H, $J = 8.2$ Hz), 6.72 (br s, 1H), 6.47 (dd, 1H, $J = 16.8$, 1.4 Hz), 5.80 (dd, 1H, $J = 11.7$, 1.4 Hz), 3.60 (br s, 1H), 2.79 (d, 1H, $J = 12.0$ Hz), 2.47 (s, 3H), 1.93–1.60 (m, 5H), 1.17–1.12 (m, 1H), 1.03 (s, 6H), 0.63 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 165.0, 146.3, 134.6, 130.0, 129.0, 127.7, 70.2, 60.1, 52.7, 47.4, 34.8, 28.9, 26.9, 21.8, 20.3, 19.9; HRMS (EI): calcd for $C_{20}H_{24}N_2O_4S$, 388.1458; found, 388.1456. Crystal data for **1n** at 25 °C: $C_{20}H_{24}N_2O_4S$, $M = 388.47$, monoclinic, $P2_12_12_1$, $a = 12.4010(7)$ Å, $b = 6.6250(4)$ Å, $c = 23.8760(17)$ Å, $V = 1961.6(2)$ Å^3, $Z = 4$, $D_c = 1.315$ Mg/m^3, $\mu = 0.193$ mm^{-1}, 12,175 reflections, 245 parameters, $R = 0.1886$, $Rw = 0.2369$.

4.2.13. 4-Methylacryloyl-10,10-dimethyl-3-(toluene-4-sulfonyl)-3,4-diaza-tricyclo[5.2.1.0^{1,5}]decan-2-one 1o. Yield 80%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (m, 2H), 7.37 (d, 2H $J = 8.0$ Hz), 7.02 (m, 1H), 6.42 (s, 1H), 3.58 (s, 1H), 2.78 (d, 1H, $J = 9.0$ Hz), 2.47 (s, 3H), 2.04–1.86 (m, 7H), 1.17 (s, 1H), 1.03 (s, 6H), 0.54 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0, 165.6, 146.1, 143.1, 134.6, 129.0, 128.9, 70.1, 122.1, 52.6, 47.3, 33.8, 28.8, 26.8, 21.7, 20.2, 19.9, 18.2; HRMS (EI): calcd for $C_{21}H_{26}N_2O_4S$, 402.1613; found, 402.1622.

4.3. Typical procedure for the synthesis of *N*-phthalimidoaziridines 2 and 3

To a solution of *exo*-10,10-diphenyl-2,10-camphanediol derived acrylate **1a** (0.20 g, 0.53 mmol) and *N*-aminophthalimide (0.12 g, 0.80 mmol) in dry THF (5.0 mL) was added lead tetraacetate (0.38 g, 0.85 mmol) in one portion under an N_2 atmosphere at 0 °C. The mixture was allowed to stir for 15 min and then quenched with water (25 mL) and extracted with dichloromethane (3 × 25 mL). The organic layers were separated and washed with brine, dried

over $MgSO_4$, and concentrated in vacuo to give the crude products. Purification by flash column chromatography eluted with hexanes/ethyl acetate = 4:1 yielded the desired aziridines **2a** and **3a** (0.26 g; 90%, ratio of diastereomers 94:06) as a white solid.

4.3.1. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-aziridine-(2*R*)-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2a. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.00–7.51 (m, 8H), 7.32–7.08 (m, 6H), 5.28 (dd, 1H, $J = 8.4$, 3.8 Hz), 4.01 (s, 1H), 2.91 (dd, 1H, $J = 7.8$, 5.4 Hz), 2.62 (dd, 1H, $J = 7.8$, 1.8 Hz), 2.48 (dd, 1H, $J = 5.4$, 1.8 Hz), 2.39–2.21 (m, 1H), 2.02–1.51 (m, 8H), 1.29–0.85 (m, 1H), 0.66 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.6, 164.3, 148.9, 143.5, 134.4, 134.3, 134.0, 130.0, 128.6, 128.4, 128.1, 128.0, 126.9, 126.8, 126.5, 126.2, 125.9, 123.6, 123.4, 123.0, 82.7, 60.3, 59.1, 51.5, 51.3, 47.7, 39.5, 38.3, 36.5, 31.0, 26.9, 24.4, 22.5, 22.4, 20.9, 14.1; HRMS (EI): calcd for $C_{33}H_{32}N_2O_5$, 536.2311; found, 536.2308.

4.3.2. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(3*S*)-methyl-aziridine-(2*R*)-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2b. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.84–7.59 (m, 8H), 7.28–7.10 (m, 6H), 5.34–5.08 (dd, 1H, $J = 8.0$, 3.6 Hz), 3.62 (s, 1H), 3.12 (d, 1H, $J = 5.2$ Hz), 2.88 (m, 1H), 2.67 (d, 1H, $J = 4.8$ Hz), 2.60 (m, 1H), 2.39–2.18 (m, 1H), 2.01–1.53 (m, 7H), 1.42–0.86 (m, 7H), 0.70–0.59 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.7, 165.4, 164.7, 164.4, 149.3, 143.7, 143.1, 134.3, 133.9, 130.4, 130.3, 128.6, 128.5, 128.0, 126.9, 126.8, 126.5, 126.3, 126.1, 125.9, 123.3, 122.9, 82.7, 82.3, 81.3, 81.2, 59.3, 59.1, 51.5, 51.4, 47.7, 44.8, 44.1, 43.1, 38.3, 37.2, 31.3, 31.1, 26.9, 24.6, 22.5, 22.4, 16.0, 12.2; HRMS (EI): calcd for $C_{34}H_{34}N_2O_5$, 550.2468; found, 550.2477; Crystal data for **2b** at 25 °C: $C_{34}H_{34}N_2O_5$, $M = 550.65$, monoclinic, $P2_12_12_1$, $a = 13.1296(18)$ Å, $b = 14.529(9)$ Å, $c = 15.1369(12)$ Å, $V = 2881.3(18)$ Å^3, $Z = 4$, $D_c = 1.269$ Mg/m^3, $\mu = 0.09$ mm^{-1}, 5472 reflections, 738 parameters, R=0.061, $Rw = 0.118$.

4.3.3. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(3*S*)-ethyl-aziridine-(2*R*)-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2c. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.84–7.59 (m, 8H), 7.27–7.10 (m, 6H), 5.13–5.07 (dd, 1H, $J = 8.1$, 3.5 Hz), 3.68 (s, 1H), 2.96 (m, 1H), 2.73 (d, 1H, $J = 4.8$ Hz), 2.34–2.16 (m, 1H), 1.98–1.42 (m, 9H), 1.29–0.83 (m, 5H), 0.79–0.65 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.8, 164.4, 149.3, 143.1, 134.3, 133.9, 130.3, 130.2, 128.6, 128.4, 128.0, 126.9, 126.8, 126.4, 126.3, 126.1, 125.8, 123.3, 122.9, 82.8, 81.3, 59.1, 51.5, 49.9, 47.7, 43.7, 37.2, 31.2, 26.9, 24.5, 24.0, 22.5, 22.4, 11.3, 10.2; HRMS (EI): calcd for $C_{35}H_{36}N_2O_5$, 564.2624; found, 564.2636; Anal. Calcd for $C_{35}H_{36}N_2O_5$: C, 74.45; H, 6.43; N, 4.96. Found: C, 74.78; H, 6.33; N, 4.67.

4.3.4. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(3*S*)-propyl-aziridine-(2*R*)-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2d. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.84–7.60 (m, 8H), 7.27–7.09 (m, 6H), 5.11 (dd, 1H, $J = 8.0$, 3.6 Hz), 3.68 (s, 1H), 2.99 (m, 1H), 2.71 (d, 1H, $J = 4.6$ Hz), 2.34–2.20 (m, 1H), 1.97–1.41 (m, 11H), 1.17–0.64 (m, 5H), 0.68 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.8, 164.4, 149.3, 143.2, 134.3, 134.0, 130.2, 128.6, 128.5, 128.0, 126.9, 126.8, 126.5, 126.3, 125.9, 123.3, 122.9, 82.9, 81.4, 59.2, 51.5, 48.6, 47.7, 44.0, 37.2, 33.0, 31.2, 26.9, 24.5, 22.5, 19.4, 13.9; HRMS (EI): calcd for $C_{36}H_{38}N_2O_5$ 578.2781. Found 578.2795. Anal. Calcd for $C_{36}H_{38}N_2O_5$: C, 74.72; H, 6.62; N, 4.84. Found: C, 74.74; H, 6.40; N, 4.63; Crystal data for **2d** at 25 °C: $C_{36}H_{38}N_2O_5$, $M = 578.70$, orthorhombic, $P2_12_12_1$, $a = 10.8763(20)$ Å, $b = 14.442(4)$ Å, $c = 19.914(6)$ Å, $V = 3127.9(14)$ Å^3, $Z = 4$, $D_c = 1.229$ Mg/m^3, $\mu = 0.08$ mm^{-1}, 3085 reflections, 389 parameters, $R = 0.044$, $Rw = 0.064$.

4.3.5. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(3*S*)-isopropyl-aziridine-(2*R*)-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2e. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.78–7.55 (m, 8H), 7.26–7.07 (m, 6H), 5.09 (dd, 1H, $J = 8.1$, 3.5 Hz), 3.77 (s, 1H), 2.97 (dd, 1H, $J = 7.8$, 5 Hz), 2.78 (d, 1H, $J = 5.0$ Hz), 2.35–2.21 (m, 1H), 2.01–1.50 (m, 7H), 1.28–0.84 (m, 9H), 0.66 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.8, 164.4, 149.2, 143.2, 133.9, 130.2, 128.5, 128.1, 126.9, 126.4, 126.3, 125.8, 122.8, 83.1, 81.3, 59.0, 54.0, 51.5, 47.7, 43.4, 37.2, 31.1, 30.0, 26.9, 24.5, 22.5, 19.6, 18.7; HRMS (EI): calcd for $C_{36}H_{38}N_2O_5$, 578.2781; found, 578.2791. Anal. Calcd for $C_{36}H_{38}N_2O_5$: C, 74.72; H, 6.62; N, 4.84. Found: C, 74.50; H, 6.61; N, 4.70; Crystal data for **2e** at 25 °C: $C_{36}H_{38}N_2O_5$, $M = 578.70$, orthorhombic, $P2_12_12_1$, $a = 8.745(4)$ Å, $b = 24.056(7)$ Å, $c = 14.938(4)$ Å, $V = 3093.6(18)$ Å^3, $Z = 4$, $D_c = 1.243$ Mg/m^3, $\mu = 0.08$ mm^{-1}, 5802 reflections, 775 parameters, $R = 0.044$, $Rw = 0.076$.

4.3.6. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(3*S*)-phenyl-aziridine-(2*R*)-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2f. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.85–7.59 (m, 8H), 7.55–7.32 (m, 4H), 7.24–7.03 (m, 7H), 5.15 (dd, 1H, $J = 8.2$, 3.4 Hz), 3.91 (d, 1H, $J = 5.2$ Hz), 3.61 (s, 1H), (3.17, 1H, d, $J = 5.2$ Hz), 2.32–2.19 (m, 1H), 2.03–1.55 (m, 8H), 1.28–0.87 (m, 1H), 0.70 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 164.6, 163.8, 149.1, 143.0, 134.2, 134.1, 130.3, 129.6, 128.8, 128.6, 128.4, 128.1, 127.4, 127.0, 126.8, 126.5, 126.3, 126.0, 125.8, 123.1, 83.1, 81.3, 59.4, 51.5, 49.7, 47.8, 45.8, 37.3, 31.5, 31.3, 29.0, 26.9, 24.6, 22.6, 22.4, 14.0, 11.3; HRMS (EI): calcd for $C_{39}H_{36}N_2O_5$, 612.2624; found, 612.2622; Crystal data for **2f** at 25 °C: $C_{29}H_{36}N_2O_5$, $M = 612.72$, orthorhombic, $P2_12_12_1$, $a = 13.206(3)$ Å, $b = 17.93(1)$ Å, $c = 30.597(7)$ Å, $V = 7246(5)$ Å^3, $Z = 8$, $D_c = 1.123$ Mg/m^3, $\mu = 0.07$ mm^{-1}, 6994 reflections, 830 parameters, $R = 0.138$, $Rw = 0.194$.

4.3.7. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-2-methyl-aziridine-(2*R*)-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2g. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.85–7.60 (m, 8H), 7.38–7.12 (m, 6H), 5.30–5.14 (dd, 1H, $J = 8.2$, 3.5 Hz), 4.23 (s, 1H), 3.66 (s, 1H), 2.97 (d, 1H, $J = 1.8$ Hz), 2.82 (s, 1H), 2.47 (d, 1H, $J = 1.8$ Hz), 2.39–2.20 (m, 1H), 2.00–1.53 (m, 10H), 1.34–0.62 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 167.8, 165.7, 165.4, 164.7, 149.1, 148.6, 143.8, 143.2,

134.3, 133.9, 130.4, 130.3, 128.7, 128.5, 128.1, 128.0, 126.9, 126.8, 126.6, 126.6, 126.3, 126.0, 123.3, 122.9, 83.2, 82.6, 81.5, 81.3, 59.2, 59.0, 51.6, 51.2, 47.7, 44.4, 43.8, 43.6, 41.7, 38.5, 37.0, 31.3, 30.9, 27.0, 24.4, 24.3, 22.7, 22.5, 18.5, 13.4; HRMS (EI): calcd for $C_{34}H_{34}N_2O_5$, 550.2468; found, 550.2451; Anal. Calcd for $C_{34}H_{34}N_2O_5$: C, 74.16; H, 6.22; N, 5.09. Found: C, 73.95; H, 6.08; N, 4.93.

4.3.8. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(2*R*,3*S*)-dimethyl-aziridine-2-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2h. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.58 (m, 8H), 7.27–7.09 (m, 6H), 5.17 (dd, 1H, $J = 8.1$, 3.5 Hz), 3.62 (s, 1H), 3.04 (qd, 1H, $J = 5.8$, 0.8 Hz), 2.32–2.17 (m, 1H), 1.93–1.84 (m, 4H), 1.70–1.51 (m, 7H), 1.37–1.29 (d, 3H, $J = 5.8$ Hz), 1.16–0.85 (m, 1H), 0.71 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.2, 164.7, 149.1, 143.1, 134.2, 133.8, 130.5, 128.5, 127.9, 126.9, 126.5, 126.3, 126.0, 123.2, 122.8, 82.7, 81.4, 60.3, 59.2, 51.5, 51.1, 49.5, 47.9, 47.7, 37.0, 31.4, 27.0, 24.5, 22.4, 21.0, 14.0, 12.24; HRMS (EI): calcd for $C_{35}H_{36}N_2O_5$, 564.2624; found, 564.2622. Anal. Calcd for $C_{35}H_{36}N_2O_5$: C, 74.45; H, 6.43; N, 4.96. Found: C, 74.18; H, 6.21; N, 4.84; Crystal data for **2h** at 25 °C: $C_{35}H_{36}N_2O_5$, $M = 564.67$, orthorhombic, $P2_12_12_1$, $a = 6.842(6)$ Å, $b = 16.215(3)$ Å, $c = 25.986(5)$ Å, $V = 2883(3)$ Å^3, $Z = 4$, $D_c = 1.301$ Mg/m^3, $\mu = 0.09$ mm^{-1}, 2897 reflections, 380 parameters, $R = 0.055$, Rw=0.097.

4.3.9. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(3*S*)-ethyl-(2*R*)-methyl-aziridine-2-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2i. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.76–7.58 (m, 8H), 7.26–7.07 (m, 6H), 5.16 (dd, 1H, $J = 8.1$, 3.5 Hz), 3.68 (s, 1H), 3.06 (t, 1H, $J = 7.1$ Hz), 2.32–2.18 (m, 1H), 1.99–1.81 (m, 2H), 1.77–1.33 (m, 12H), 1.08–1.01(m, 3H), 0.69 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.2, 164.7, 149.2, 143.2, 133.8, 130.4, 128.5, 128.0, 126.9, 126.4, 126.3, 125.9, 122.7, 82.9, 81.4, 60.3, 59.1, 54.9, 51.5, 48.0, 47.7, 36.9, 31.3, 27.0, 24.4, 22.5, 20.9, 14.1, 13.9, 10.9; HRMS (EI): calcd for $C_{36}H_{38}N_2O_5$, 578.2781; found, 578.2764. Anal. Calcd for $C_{36}H_{38}N_2O_5$: C, 74.72; H, 6.62; N, 4.84. Found: C, 74.66; H, 6.62; N, 4.65.

4.3.10. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-3,3-dimethyl-aziridine-2*S*-carboxylic acid 1-(hydroxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2j. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.90–7.58 (m, 8H), 7.30–7.08 (m, 6H), 5.34–5.28 (dd, 1H, $J = 7.6$, 3.9 Hz), 3.98 (s, 1H), 3.17 (s, 1H), 2.39–2.25 (m, 1H), 2.12–1.93 (m, 1H), 1.72–1.40 (m, 3H), 1.60 (s, 3H), 1.26–0.88 (m, 2H), 1.29 (s, 3H), 1.10 (s, 3H), 0.64 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.3, 165.3, 149.6, 143.7, 134.2, 130.5, 128.5, 128.0, 126.8, 126.5, 126.2, 123.2, 83.0, 81.3, 58.9, 51.5, 49.7, 49.4, 47.7, 38.8, 31.1, 26.9, 24.6, 22.6, 19.8, 18.5; HRMS (EI): calcd for $C_{35}H_{36}N_2O_5$, 564.2624; found, 564.2634. Anal. Calcd for $C_{35}H_{36}N_2O_5$: C, 74.45; H, 6.43; N, 4.96. Found: C, 74.18; H, 6.29; N, 4.92.

4.3.11. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-(3*S*)-methyl-aziridine-(2*R*)-carboxylic acid 1-(methoxy-diphenyl-methyl)-7,7-dimethyl-bicyclo[2.2.1]hept-2-yl ester 2k. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.02–7.42 (m, 8H), 7.38–7.14 (m, 6H), 4.77 (dd, 1H, $J = 7.9$, 3.5 Hz), 3.21–2.61 (m, 2H), 2.82 (s, 3H), 2.48 (d, $J = 5.0$ Hz, 1H), 1.88–1.22 (m, 4H), 1.49 (d, 3H, $J = 5.4$ Hz), 1.14–0.66 (m, 2H), 1.14 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.2, 164.8, 140.5, 138.9, 133.9, 131.5, 130.3, 129.7, 129.5, 128.4, 127.4, 127.0, 126.8, 123.3, 122.9, 117.9, 87.6, 81.6, 61.2, 52.3, 49.9, 49.2, 45.1, 44.4, 37.8, 31.5, 25.5, 23.6, 22.6, 16.3, 14.0.

4.3.12. 2-{2-[10,10-Dimethyl-2-oxo-3-(toluene-4-sulfonyl)-3,4-diaza-tricyclo[5.2.1.0^{1,5}]decane-4-carbonyl]-(2*R*)-aziridin-1-yl}-isoindole-1,3-dione 2n. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (br s, 2H), 7.78 (dd, 2H, $J = 8.0$, 3.0 Hz), 7.70 (dd, 2H, $J = 8.0$, 3.0 Hz), 7.37 (d, 2H, $J = 8.1$ Hz), 3.71 (br s, 1H), 3.56 (br s, 1H), 3.02 (br s, 1H), 2.96 (d, 2H, $J = 6.6$ Hz), 2.48 (s, 3H), 1.97–1.88 (m, 4H), 1.42 (s, 3H), 1.15 (br s, 1H), 1.09 (s, 3H), 0.42 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4, 166.7, 164.3, 146.9, 134.2, 130.3, 130.1, 129.1, 123.2, 71.0, 60.2, 53.0, 47.5, 40.3, 38.5, 34.0, 29.2, 27.0, 21.8, 20.7, 20.4; HRMS (EI): calcd for $C_{28}H_{28}N_4O_6S$, 548.1724; found, 548.1721. Crystal data for **2n** at 25 °C: $C_{28}H_{28}N_4O_6S$, $M = 548.60$, orthorhombic, $P2_12_12_1$, $a = 6.7301(2)$ Å, $b = 14.1264(4)$ Å, $c = 27.8317(9)$ Å, $V = 2640.02(14)$ Å^3, $Z = 4$, $D_c = 1.377$ Mg/m^3, $\mu = 0.173$ mm^{-1}, 10,184 reflections, 353 parameters, $R = 0.0934$, $Rw = 0.1526$.

4.3.13. 2-{2-[10,10-Dimethyl-2-oxo-3-(toluene-4-sulfonyl)-3,4-diaza-tricyclo[5.2.1.0^{1,5}]decane-4-carbonyl]-(3*S*)-methyl-2*R*-aziridin-1-yl}-isoindole-1,3-dione 2o. Inseperable *N*-invertomer mixture of diastereomers were obtained. Selected peaks were shown.[1] H NMR (400 MHz, $CDCl_3$) δ 7.66–7.63 (m, 2H), 7.38 (br s, 1H), 7.27(s, 1H), 3.64 (s, 1H), 3.61 (qd, 1H, $J = 5.6$, 5.6 Hz), 3.55 (br s, 1H), 3.29 (br s, 1H), 3.06 (qd, 1H, $J = 5.6$ 5.6 Hz), 2.98 (d, 1H, $J = 13.5$ Hz), 1.08 (s, 6H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 167.0, 166.4, 165.3, 146.7, 134.5, 134.2, 134.1, 134.0, 133.7, 130.4, 130.2, 129.1, 129.0, 123.4, 123.1, 122.8, 71.0, 67.1, 60.1, 53.0, 47.5, 47.3, 45.6, 45.2, 44.2, 34.0, 29.7, 29.2, 28.8, 27.0; MS (EI) (%): calcd for $C_{29}H_{30}N_4O_6S$, 562.1886; found, 562.4 (5), 406.9 (20), 379.0 (30), 260.2 (50), 247.0 (60), 229.0 (100), 201.2 (75), 155.1 (65).

4.3.14. 1-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-aziridine-(2*R*)-carboxylic acid methyl ester 4a. To a solution of **2a** (0.10 g, 0.19 mmol) in MeOH (2.0 mL), was added sodium methoxide (40 mg, 0.74 mmol) in one portion at ambient temperature. The reaction was quenched with water (25 mL) after 3 h and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The crude product was purified further by flash column chromatography using hexanes/ethyl acetate = 6:1 as a eluent to afford pure product **4a** (30 mg, 67%) and the auxiliary **A** was recovered with 85% yield. Compound **4a**: $[\alpha]_D = +109.5$ (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.78–7.66 (m, 4H), 3.81 (s, 3H), 3.17 (dd, 1H, $J = 7.6$, 5.8 Hz), 2.82 (dd, 1H, $J = 7.6$, 1.6 Hz), 2.84 (dd, 1H, $J = 5.8$, 1.6 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.5, 164.5, 134.3, 129.9, 123.3, 52.7, 39.7, 36.4; HRMS (EI): calcd for $C_{12}H_{10}N_2O_4$, 246.0624; found, 246.0641.

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